

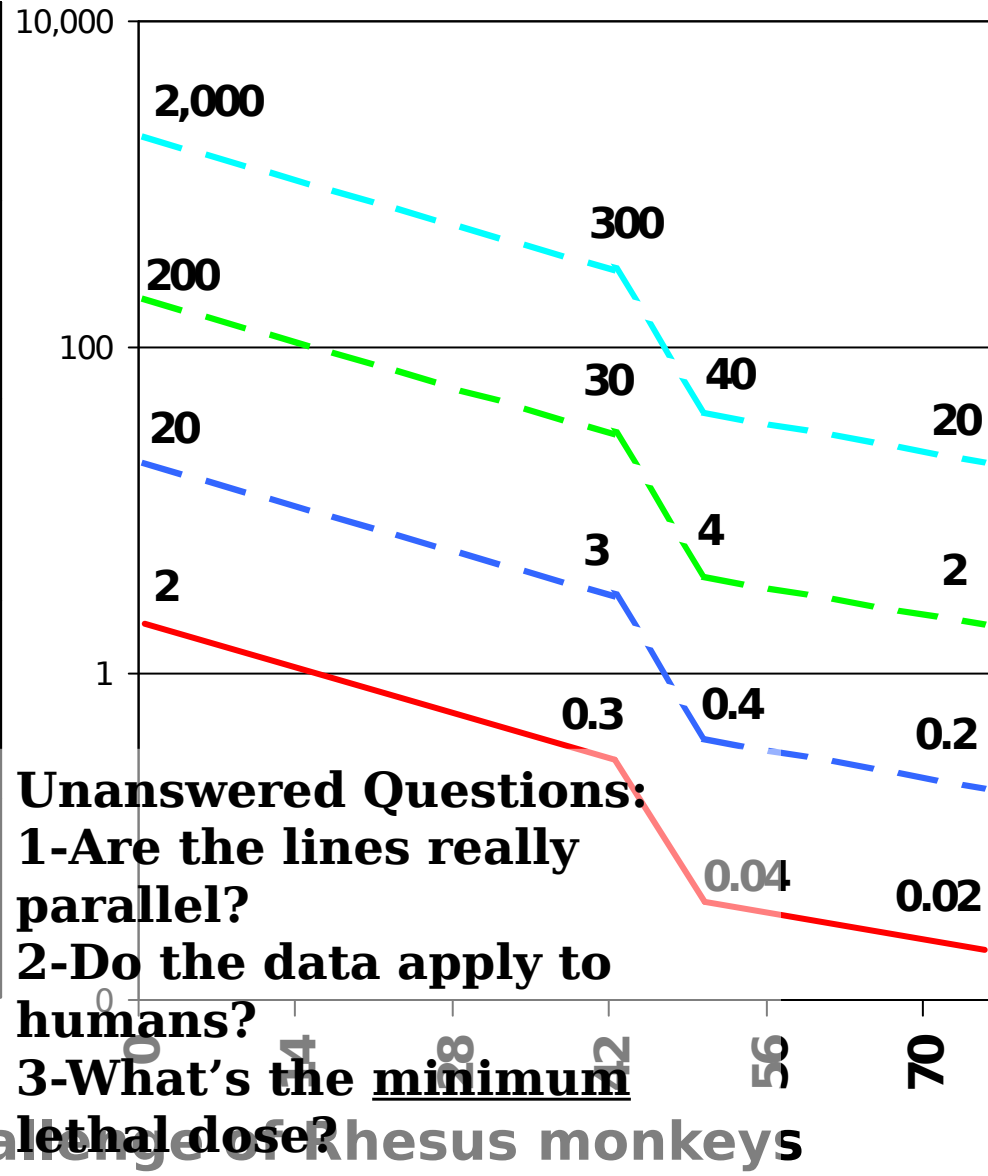
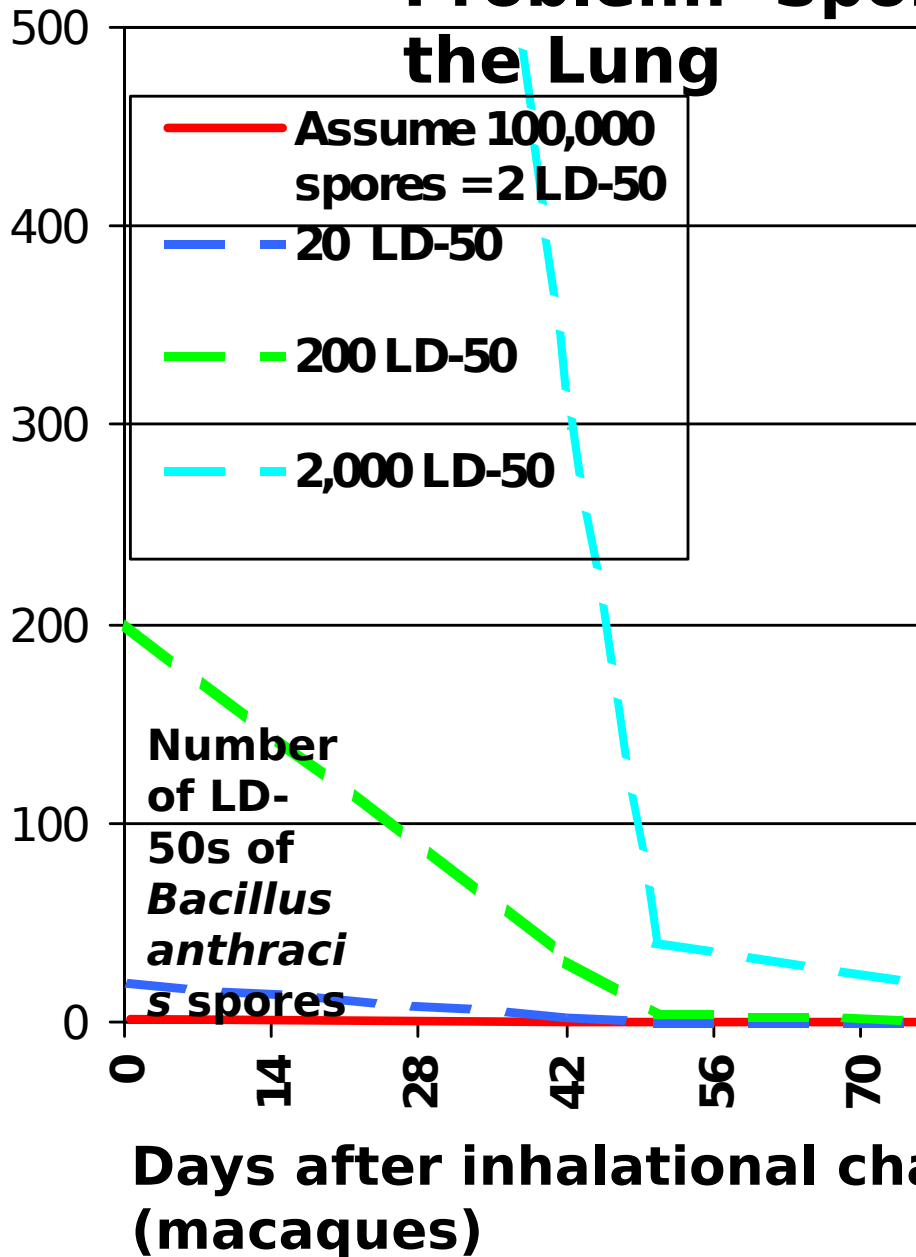
***Department of Defense
Anthrax Vaccine
Immunization Program***

Armed Forces Epidemiological Board

**Update on Anthrax
Vaccinations**

LTC John D. Grabenstein, RPh, PhD

Problem: Spores Persisting in the Lung



Red line from Henderson, Peacock, Belton. *Journal of Hygiene* 1956;54:28-36.
 Blue and green lines speculate on high-dose exposure, based on DRES-Canada experiment



Is Anthrax Vaccine Licensed?

1. Simple answer: Yes, licensed on November 4, 1970.

2. Complete answer:		
	Licensed	Investigational
Product & Its Use	Pre-exposure in a 6-dose series	Post-exposure in a 3-dose series ("off-label")
Manufacturing Facility, Process	Michigan - 1970-98+ BioPort (2002)	BioPort - 2001
Lots vis-à-vis FDA Release Specs	Lots used by DoD 1970 to present FAV063 (Feb 02)	FAV063 (Dec 01)



Steps to FDA Release of AVA

- **FDA approves revised potency test (Jul/Nov 01) ✓**
- **FDA approves Lansing renovations (27 Dec 01) ✓**
 - **FDA accepts post-marketing commitments (Jan 02) ✓**
- **FDA approves contract packager/filler (Hollister- Stier Laboratories, Spokane) (31 Jan 02) ✓**
 - **FDA accepts post-marketing commitments ✓**
- **FDA approval of BioPort's stability studies (31 Jan 02) ✓**
- **FDA approval of revised product labeling (31 Jan 02) ✓**
- **FDA review of lot-release tests for three "exhibit" or consistency lots (all passing) (31 Jan 02) ✓**



Independent Scientific

- **Panel on Review of Bacterial Vaccines & Toxoids,**
advising FDA, 1978-85, *Fed Reg*
- 1985;50:51002-117
- **Armed Forces Epidemiological Board (AFEB),**
advising DoD, 1994 to present
- **Cochrane Collaboration, Oxford, Vaccine**
- 1998;16:880-4
- **Working Grp on Civ. Biodefense, JAMA**
- 1999;281:1735-45.
- **Advisory Committee on Immunization Practices (ACIP),** advising CDC, Jul 2000 (*MMWR*
- 2000;49(RR-15):1-20)
- **Anthrax Vaccine Expert Committee (AVEC),**
reaching independent judgments, 1998 to



Institute of Medicine Committee

- **Institute of Medicine Committee to Assess the Safety and Efficacy of the Anthrax Vaccine**
- **Brian L. Strom, MD, MPH (chair), U. Pennsylvania**
William E. Barlow, PhD, Group Health Cooperative, U. Washington
Dan G. Blazer, II, MD, MPH, PhD, Duke University
Linda D. Cowan, PhD, University of Oklahoma
Kathryn M. Edwards, MD, Vanderbilt University
Denise L. Faustman, MD, PhD, Harvard Medical School
Emil C. Gotschlich, MD, Rockefeller University
Dennis L. Kasper, MD, Harvard Medical School
Don P. Metzgar, PhD, retired from Connaught Laboratories
Hugh H. Tilson, MD, DrPH, University of North Carolina

- **Public Meetings: Oct 00, Jan 01, Apr 01, Jul 01**
Closed session: Nov 01. Review: Jan-Feb 02
Report likely to be released early Mar 02



Anthrax Vaccine Safety Litany

- **Brachman Study, *Am J Public Health* 1962; 52:632-45 (n = 379)**
- **CDC Observational Study, *Fed Reg* 1985; 50:51002-117 (6,986)**
- **Ft Detrick Multi-Vaccine Studies, *BJHH* '58, *Ann Intern Med* '65; '74;81:594-600 (99)**
- **Fort Detrick Special Immunization Program, *Vaccine* 2001; 20:972-8 (1,583)**
- **Fort Bragg Booster Study (after Persian Gulf War), *Vaccine* 2002; in press (495)**
- **USAMRIID Reduced-Dose / Route-Change Study, *Vaccine* 2002; in press (173)**
- **Canadian Forces Safety Survey, manuscript in progress (576)**
- **TAMC-601 Survey, *MMWR* 2000; 49:341-5, additional manuscript in progress (601)**
- **US Forces Korea Records, *MMWR* 2000; 49:341-5, add'l under peer review (2,824)**
- **VAERS review by AVEC, *Pharmacoepidemiol & Drug Safety* 2002; in press (1,623)**
- **ROTC Cadets, Ft Lewis, *Med Surveil Mon Rep* 2001; 7(5):9-11 (73)**
- **USAF Air Combat Command Study, *Military Medicine* 2002; in press (4,045)**



Safety: Flight Physicals

- **US Army Aviation Epidemiology Data Register, aviator flight physicals, Fort Rucker, Alabama**
- No differences between 3,386 matched pairs:
 - anthrax vaccinated or unvaccinated, before or after.
 - Hearing loss, (> 15 decibel hearing loss, any frequency, either ear)
 - Weight loss or gain of 20 pounds or more
 - Hypertension ($\geq 140/90$ or began taking antihypertensive medication)
 - Abnormal change in blood pressure
 - Abnormal hematocrit
 - Intraocular hypertension (≥ 21 or began taking medication for glaucoma)
 - Stereopsis greater than 40-second arc
 - Abnormal stereopsis
 - Loss of vision of ≥ 1 , ≥ 2 , or ≥ 3 more Snellen lines
 - Development of proteinuria, glycosuria, or hematuria



Prospective Clinical Trial

- **Dose-reduction, Route-change, Gender-effect Study, n ~ 1,600, Mar 02 - late 06/early 07**

Parties: CDC, Baylor College of Medicine, Emory U., Mayo Clinic,

- **WRAIR, U Alabama -Birmingham, and partners**

Hypotheses: Are fewer doses as

- **immunogenic? Is IM less reactogenic than SC? Do women differ from men? Correlates of protection?**

Status: Reconciling IRBs, preparing to



Additional Human Studies Underway

- **Prospective Clinical Trial: Dose, Route, Gender Study**
- **Spontaneous Reports: Anthrax Vaccine Expert**

- **Committee**

Reproductive Outcomes

Naval Health Research Center (NHRC)

Army Reproductive Outcomes (CHES)

- **Defense Women's Health Database Project (DoD)**

Long-Term Studies, Retrospective

Multiple Immunization Project (Fort Detrick, Maryland)

Special Immunization Program (USAMRIID)

Disability Discharge Database Study (USARIEM)

- **using Total Army Injury & Health Outcomes Database (TAIHOD)**

Long-Term Studies, Prospective

Defense Medical Surveillance System (DMSS)

Naval Health Research Center (NHRC)

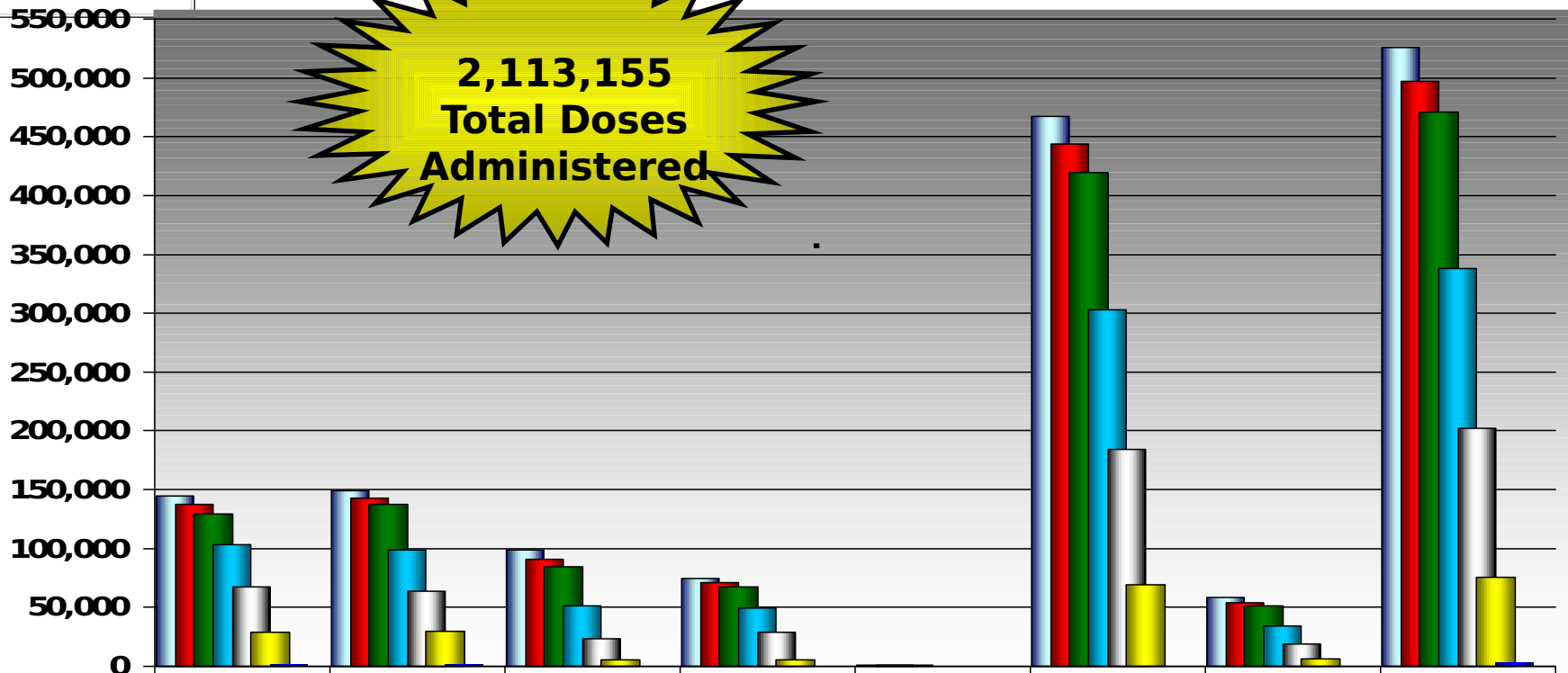
- **Aviation Epidemiology Data Register (AEDR)**

Millennium Cohort Study



Total Force Anthrax Immunization Status

**2,113,155
Total Doses
Administered**



	ARMY	AIR FORCE	NAVY	MARINES	COAST GUARD	TOTAL (current program)	ARCHIVED IMMUNIZATIONS	TOTAL IMMUNIZATIONS
DOSE #1	144,897	149,055	98,426	74,426	672	467,476	58,670	526,146
DOSE #2	137,347	143,123	91,006	71,437	639	443,552	53,853	497,405
DOSE #3	129,090	137,084	84,895	67,591	604	419,264	51,634	470,898
DOSE #4	103,552	98,575	51,151	49,260	396	302,934	34,576	337,510
DOSE #5	67,556	64,066	23,642	28,679	159	184,102	18,477	202,579
DOSE #6	28,619	29,967	5,605	4,999	27	69,217	6,072	75,289
BOOSTER	1,597	1,591	3	1	0	3,192	136	3,328
TOTAL	612,658	623,461	354,728	296,393	2,497	1,889,737	223,418	2,113,155

ALL DATA FROM DEERS 31 JAN



- **Policy Options**

- **Post-exposure vaccination only**
- **Vaccination for special mission units, research only**
- **Vaccination of DoD personnel in high risk areas**
- • **Vaccination of forces most vulnerable during opns**
- **Vaccination for Total Force**
- **Enhanced attention:**
 - **SC injection site: over deltoid rather than triceps**
- • **Not vaccinating women who might be pregnant**
- **Precision of vaccination dates entered into**